

Editorial Comment

Myocardial Stunning in Hypertrophic Cardiomyopathy?*

ANDRÉ PASTERNAK, MD, FACC

Montreal, Quebec, Canada

Myocardial perfusion abnormalities occur commonly in patients with hypertrophic cardiomyopathy presenting with or without angina and with or without dysfunction (1-5). O'Gara et al. (5) identified regional perfusion defects after maximal exercise in 57% of patients. The majority of the patients had a reversible defect; a fixed defect was observed predominantly in patients with depressed left ventricular function at rest. Correlatively, a spectrum of left ventricular wall motion abnormalities ranging from abnormal left ventricular diastolic mechanics (6) to segmental systolic abnormalities (7) and transmural myocardial infarction (8), often silent, has been reported in patients with hypertrophic cardiomyopathy and normal coronary arteries. These abnormalities may lead, although infrequently, to progression into a segmental or generalized hypokinetic left ventricle, with ventricular dilation and heart failure (7-10).

Current study. In this issue of the Journal, Fine and coworkers (11) report the history of a young woman with mildly obstructive hypertrophic cardiomyopathy presenting with chest pain, electrocardiographic abnormalities suggestive of myocardial infarction and evidence of an apical aneurysm by echocardiography, radionuclide and contrast ventriculography in the presence of normal coronary arteries. Verapamil therapy was started, and 13 days after admission single photon emission computed tomographic imaging (SPECT) revealed normal perfusion of the area shown to be aneurysmal 5 days earlier. In the following weeks, ventricular contraction returned progressively to normal. The authors suggest that the reversibility of the wall motion abnormality with the relief of ischemia might be predicted by SPECT scintigraphy. Thus, this study documents that reversible systolic wall motion abnormalities do occur in patients with hypertrophic cardiomyopathy concomitant with transient severe regional ischemia. In addition, sequen-

tial echocardiograms showed the persistence of wall motion abnormalities after the normalization of myocardial perfusion with delayed but complete functional recovery; this truly represents "myocardial stunning" (12). However, the lack of simultaneous assessment of myocardial perfusion and of left ventricular wall dynamics as well as the absence of sequential evaluation of myocardial perfusion may limit the validity of these conclusions. Thus, it would have been helpful to obtain an at rest thallium SPECT study on admission when the patient was symptomatic; we can presume that it would have shown a regional perfusion defect in the aneurysmal area.

The normalcy of the (at rest ?) SPECT study done on the 13th day after admission on verapamil therapy implies that in the area of the apical dysfunction observed on admission there was now adequately perfused and viable tissue suggesting a favorable functional prognosis. Although no wall motion study was done at the time of the normal thallium imaging, some regression of the apical dysfunction would probably have been apparent. A recent study by Stratton et al. (13) in patients with prior myocardial infarction has addressed the issue of the correlation between regional wall motion abnormalities and the severity of the tomographic thallium perfusion defects. Overall, there was an excellent correlation, but discrepancies were noted and wall motion abnormalities affected more of the ventricle than did perfusion abnormalities. Thus, among regions with no defect or a very small defect, 6% demonstrated echocardiographic akinesia or dyskinesia, or both. The explanation for the discrepancy remains unclear. Similarly, Massie et al. (14) noted that 11% of regions with normal thallium uptake had abnormal wall motion. Indeed, it would have been helpful to repeat the thallium study at 6 weeks after hospital discharge, when there was resolution of the wall motion abnormalities to document whether subtle change in thallium kinetics had not occurred when compared with the "normal" thallium perfusion—in particular, in the early acquisitions.

Significance of myocardial ischemia and myocardial stunning in patients with hypertrophic cardiomyopathy. The vulnerability to myocardial ischemia in patients with hypertrophic cardiomyopathy has been well documented by coronary flow studies showing a reduced myocardial perfusion for unit left ventricular mass and increased coronary resistance at rest (15,16) with inadequate coronary reserve during pacing stress (17,18). This chronic hypoperfusion may result in progressive impairment of ventricular function, in particular subendocardial, and may cause focal necrosis and fibrosis. In contrast, "myocardial stunning" (12,19) results from an acute and transient ischemic event but it may persist for weeks after the restoration of adequate myocardial perfusion with eventual recovery to normal function. This has been

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From the Department of Medicine, Montreal Heart Institute and the Department of Medicine, University of Montreal, Montreal, Quebec, Canada.

Address for reprints: André Pasternak, MD, Department of Medicine, Montreal Heart Institute, 5000 East Bélanger Street, Montreal, Quebec, Canada HIT 1C8.

reported in experimental models of brief transient periods of coronary occlusion followed by reperfusion (20), and in clinical settings of transient ischemia induced by exercise or by coronary angioplasty (21) and in patients after reperfusion for acute myocardial infarction (22). Such abnormalities of myocardial contraction may occur more frequently than realized in hypertrophic cardiomyopathy because it is possible to induce silent myocardial ischemia with exercise in asymptomatic patients with this condition (23).

The mechanism of these spontaneous transient episodes of myocardial ischemia remains unclear. Along with the potential causes listed by Fine et al. (11), the role of dynamic alterations in the myocardial microcirculation must be considered (24) possibly modulated by catecholamines (25). In fact, coronary spasm, at the epicardial or arteriolar level, would constitute a clear clinical replication of the experimental settings of "myocardial stunning." The clinical episode induced by methylethylergonovine is consistent with this hypothesis. Clearly, several mechanisms may be operative here. The abnormality of calcium fluxes and calcium-antagonist receptors, possibly genetic, recently demonstrated in patients with hypertrophic cardiomyopathy (26), may affect not only cardiac tissue but also coronary and peripheral vascular smooth muscles (27,28) and may help to better understand the pathophysiology of ischemia and its therapy. Indeed, the efficacy of verapamil in improving myocardial function in this patient is noteworthy. In addition to its role in arterial (29) and arteriolar (24) spasm, verapamil improves relaxation and diastolic filling (30,31) and has been shown to diminish inducible silent ischemia in many asymptomatic patients with hypertrophic cardiomyopathy (23). It appears to be the most effective of the many drugs administered to the cardiomyopathic hamsters (32,33); it may protect against myocardial damage by inhibiting voltage-dependent calcium uptake and preventing free radical-generated lipid peroxidation and cell injury (34). Furthermore, in the experimental setting of "myocardial stunning," it has recently been shown to enhance the postischemic functional and metabolic recovery (35), in particular in left ventricular hypertrophy (36), by diminishing minimal coronary resistance and reducing or preventing the alterations in high energy metabolism.

Conclusions. This case report illustrates the central role of myocardial ischemia in hypertrophic cardiomyopathy and the dynamic relation between abnormalities of myocardial perfusion and ventricular wall motion, possibly accounting for a whole spectrum of ventricular dysfunction. On a background of chronically reduced coronary reserve, episodes of transient ischemia—either induced by stress or exercise or occurring spontaneously—may supervene, resulting in either "stunned myocardium" or myocardial infarction. The repetition of these events may result in alterations in wall dynamics, wall thickness and ventricular volume. The precise mechanism of these episodes of tran-

sient, spontaneous regional ischemia in hypertrophic cardiomyopathy remains to be elucidated, and further studies will be necessary to assess the role of prophylactic calcium antagonist therapy (37) in preventing ischemic alterations of myocardial function.

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